REMARKS

Claims 1-21, 23-27, and 29-33 are pending in this application. Claims 22 and 28 previously were canceled. Claim 1 has been amended to recite that the acidity regulating component includes a monomer and an oligomer derived from the same biodegradable polymer, which finds support in Claim 16, now cancelled. Claim 26 has been amended to delete the repeated word, "including."

This amendment is submitted to expedite prosecution only and should not be viewed as a disclaimer of subject matter. No new matter has been added by way of this amendment.

35 U.S.C. §102 Rejections

Claims 1-25 are rejected under 35 USC 102(b) as anticipated by U.S. 6,506,399 to Donovan ('399 patent). As stated above, Claim 1 has been amended to recite that the acidity regulating component includes a monomer and an oligomer derived from the same biodegradable polymer. The only other independent claims, 26 and 30, already include a similar limitation. In order to anticipate a claim, the cited reference must teach every element disclosed in the claims. Among other things, the '399 patent does not disclose an acidity regulating component that includes a monomer and an oligomer derived from the same biodegradable polymer for maintaining *in vivo* pHs of less than about 7 or the means to do so. The '399 patent discloses that suitable "pH conditions to form a complex of neurotoxin typically include pH values between about 5.0 and about 6.9. Suitable pH conditions are typically achieved through use of an aqueous buffer, such as sodium bicarbonate, as the solvent."[1] The '399 patent also discloses that "pH of the casting or other solution in which the botulinum toxin is to be mixed is maintained at pH 4.2-6.8, because at pH above about pH 7 the stabilizing nontoxin proteins can dissociate . . . ."[2] In other words, while the '399 patent discloses that making, formulating, or casting *Botulinum* toxin must be done at acidic conditions, the '399

[1] '399 Patent, col. 23, lns 54-58.
[2] '399 Patent, col. 28, lns 62-67.

patent does not direct the skilled artisan to prepare a biodegradable neurotoxin implant having a neurotoxin component associated with a biodegradable polymer component, and an acidity regulating component made from a monomer and an oligomer derived from the same biodegradable polymer and capable of maintaining an *in vivo* pH in the vicinity of the neurotoxin of less than about 7.[3] In other words, the '399 patent does not disclose a stabilized implant capable of maintaining an acidic microenvironment around the neurotoxin as the implant degrades. Since the '399 patent does not discuss maintaining *in vivo* pHs of less than about 7 or the means to do so, it is not a proper anticipation reference and the Applicant respectfully requests withdrawal of this rejection.

Claims 16-23 and 25-33 are rejected under USC 102(b) as anticipated by U.S. 6,312,708 to Donovan ('708 patent). The '708 patent is related to the '399 patent and contains similar disclosure. Like the'399 patent, the '708 patent does not disclose an acidity regulating component that includes a monomer and an oligomer derived from the same biodegradable polymer for maintaining *in vivo* pHs of less than about 7 or the means to do so. The '708 patent discloses that suitable "pH conditions to form a complex of neurotoxin typically include pH values between about 5.0 and about 6.9. Suitable pH conditions are typically achieved through use of an aqueous buffer, such as sodium bicarbonate, as the solvent."[4] The '708 patent also discloses that "pH of the casting or other solution in which the botulinum toxin is to be mixed is maintained at pH 4.2-6.8, because at pH above about pH 7 the stabilizing nontoxin proteins can dissociate . . . ."[5] Like the '399 patent, the '708 patent does not direct the skilled artisan to prepare a biodegradable neurotoxin implant having a neurotoxin component associated with a biodegradable polymer component, and an acidity regulating component made from a monomer and an oligomer derived from the same biodegradable polymer and capable of maintaining an *in vivo* pH in the vicinity of the

[3] *See* Claim 1, as amended.
[4] '708 Patent, paragraph bridging cols. 23 & 24.
[5] '708 Patent, col. 29, lns 6-11.

neurotoxin of less than about 7.[6] In other words, the '708 patent does not disclose a stabilized implant capable of maintaining an acidic microenvironment around the neurotoxin as the implant degrades. Since the '708 patent does not discuss maintaining *in vivo* pHs of less than about 7 or the means to do so, it is not a proper anticipation reference and the Applicant respectfully requests withdrawal of this rejection.

35 U.S.C. §103 Rejections

Claims 1 and 26-30 are rejected under 35 USC 103 as obvious over the '399 patent in view of Agrawal (U.S. 5,741,329). As discussed above, the '399 patent does not disclose an acidity regulating component made from a monomer and an oligomer derived from the same biodegradable polymer and capable of maintaining an *in vivo* pH in the vicinity of the neurotoxin of less than about 7. Agrawal does nothing to remedy this shortcoming. Rather, Agarwal discloses a method of controlling pH in the vicinity of biodegradable implants by buffering them with calcium carbonate, calcium hydroxyapatite, or sodium bicarbonate, among others.[7] Agrawal also teaches that alkaline agents "are preferably non-toxic and suitable for combination with a biodegradable polymer, such as polylactic acid, polyglycolic acid, . . . , copolymers thereof, or mixtures thereof."[8] Agrawal further teaches amounts of alkaline substances that are sufficient to "offset a rapid decrease in pH in the presence of acidic polymer breakdown products."[9] Agrawal's three investigated salts "were successful in controlling the decrease in pH due to the acidic degradation products"[10] of the PLA-PGA copolymer until complete degradation was achieved. In these respects, Agrawal teaches away from the present claims. The combination of the '399 patent and Agrawal does not teach every element of the present claims. Accordingly, the Applicant respectfully requests withdrawal of this rejection.

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[6] *See* Claim 1, as amended.
[7] *See* Agrawal, Abstract; Fig. 2; col. 3, lns 29-43.
[8] Agrawal, col. 3, lns 33-37.
[9] Agrawal, col. 4, lns 8-13.
[10] Agrawal, paragraph bridging cols. 7 & 8.

Claims 1 and 11-13 are rejected under 35 USC 103 as obvious over the '399 patent view of Gurny (U.S. 6,440,460). As discussed above, the '399 patent does not disclose an acidity regulating component made from a monomer and an oligomer derived from the same biodegradable polymer and capable of maintaining an *in vivo* pH in the vicinity of the neurotoxin of less than about 7. Gurny does nothing to remedy this shortcoming. Gurny simply discloses that it is necessary to maintain the pH-level of the pharmaceutical composition at "a physiologically acceptable constant range between 5.0 and 7.5."[11] The combination of the '399 patent and Gurny does not teach every element of the present claims. Accordingly, the Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Applicant respectfully requests that a timely Notice of Allowance be issued in this case. The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

Dated: 28 April 2008

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[11] Gurny, col. 2, lns 17-23.